

Remarks

Claims 1-2, 4, 6 and 9-15 are pending in this application. Claim 15 is amended for a formalistic reason, *i.e.*, to correct its dependency. No new matter is added. Applicant respectfully submits that all of the pending claims are allowable for at least the following reasons.

A. The Rejection Under 35 U.S.C. §112 Should Be Withdrawn

On pages 2-3 of the Office Action, claim 15 is rejected as allegedly indefinite “because a claim cannot depend on itself.” (Office Action, page 3). In this regard, the dependency of claim 15 is corrected by the claim amendment presented herein to make the claim depend from claim 14. In view of this amendment, Applicant respectfully requests that the rejection be withdrawn.

B. The Rejection Under 35 U.S.C. §103 Should Be Withdrawn

I. The Rejection Over Samour and Ippen Should Be Withdrawn

On pages 3-7 of the Office Action, claims 1-2, 6 and 9-13 are rejected as allegedly obvious over U.S. Patent No. 6,224,887 to Samour *et al.* (“Samour”) in view of U.S. Patent No. 4,956,370 to Ippen *et al.* (“Ippen”). In particular, it is alleged that the claims are obvious because, according to the Office Action, “[i]t would have been prima facie obvious to one of ordinary skill in the art ... to substitute the antifungal agent taught by [Samour] with substituted 2-aminothiazole which is another antifungal agent taught by [Ippen] because both antifungal agents are functionally equivalent.” (Office Action, page 7). Applicant respectfully disagrees.

On the basis of *KSR* and the Federal Circuit and District Court cases following *KSR*, the current standard of obviousness takes into account: (1) whether there would have been a “reason that would have prompted a person of ordinary skill in the relevant field to combine the elements in the way the claimed invention does;” and (2) whether the combination of elements would have yielded “predictable results” *i.e.*, whether there would have been a reasonable expectation of success. (*See e.g., PharmaStem* 491 F.3d at 1360 (“The burden falls on the patent challenger to show by clear and convincing evidence that a person of ordinary skill in the art would have had

reason to attempt to make the composition or device, or carry out the claimed process, and would have had a reasonable expectation of success in doing so.”) (emphasis added, internal quotations omitted)).

First, Applicant respectfully submits that there would have been no “reason that would have prompted a person of ordinary skill in the relevant field to combine the elements in the way the claimed invention does.” Samour describes “antifungal nail lacquer compositions” comprising: (1) at least one antifungal agent; (2) penetrating enhancers selected from the group consisting of C₇-C₁₄-hydrocarbyl substituted 1,3-dioxolane, C₇-C₁₄-hydrocarbyl substituted 1,3-dioxane and C₇-C₁₄-substituted acetal; (3) film-forming polymer; and (4) volatile solvent. (Samour, col. 3, lines 13-28). However, “examples of suitable antifungal agents” described in Samour do not include those disclosed in Ippen. Consequently, absent any disclosure in Samour that the antifungal agents described therein are disadvantageous for some reason, those skilled in the art reading Samour would not have had any reason to consider using any other antifungal agent than those described in Samour.

On the other hand, Ippen also would not have provided the “reason to combine.” Ippen discloses compositions that “may be administered locally, orally, parenterally, intraperitoneally and/or rectally, preferably parenterally, in particular intravenously,” (col. 21, lines 29-32). Ippen discloses a list more than 2 columns long of various preparations, including tablets, coated tablets, capsules, pills, granules, suppositories, solutions, suspensions and emulsions, pastes, ointments, gels, creams, lotions, powders or sprays (col. 19, line 41 to col. 21, line 68). Nothing in the list is, or even resembles, a nail lacquer. Therefore, neither Samour nor Ippen would have provided those skilled in the art with any reason to combine, and Applicant respectfully points out that the combination of Samour and Ippen is based on impermissible hindsight using the roadmap provided by the current claims. Applicant respectfully submits that no *prima facie* case of obviousness is established for this reason alone.

Second, Applicant respectfully submits that there would have been no predictability as to the properties of the formulation resulting from combining Samour and Ippen, *i.e.*, no reasonable expectation of success. As pointed out above, Samour’s description of exemplary antifungal agents does not include those compounds described in Ippen. Although it is alleged in the Office

Action that it would have been obvious to replace the antifungal agents described in Samour with those described in Ippen because “both antifungal agents are functionally equivalent,” Applicant respectfully submits that such a contention is scientifically incorrect. This is because, even if the allegation made in the Office Action regarding “functional equivalence” were true, such an allegation wholly ignores the fact that it is difficult to predict how the other ingredients in the formulation would affect the behaviour of the active agent. In other words, even assuming, *arguendo*, that the exemplary antifungal agents described in Samour and the 2-aminothiazole compounds described in Ippen were functionally equivalent, those skilled in the art would not have been able to predict that using the 2-aminothiazoles in combination with the various particular ingredients provided in Samour would be beneficial, and thus, no reasonable expectation of success would have existed.

Indeed, Applicant respectfully points out that, based on the structures of 2-aminothiazoles recited by the pending claims, those skilled in the art would not have expected that the compounds would be compatible with polar ingredients, some of which are used in the formulations described in Samour. To be more specific, those skilled in the art would have expected that the 2-aminothiazole compounds would bind to those polar ingredients, which would result in inactivation. In this regard, a post-priority reference indeed confirms that Abafungin, an antifungal agent used throughout the examples provided in the current specification, “exerts a fungicidal activity preferably in defined minimal media or slightly enriched liquid media at a pH range of 4.0-5.5.” (*See Borelli et al., Chemotherapy*, 54: 245-259 (2008), a copy of which is attached hereto as **Exhibit A**, at page 251, left column). Despite this expectation, it was surprisingly and successfully demonstrated that Abafungin, in the presence of polar ingredients recited by the current claims, could be used to substantially improve the symptoms of a fungal infection within 45 days of treatment, and that it is likely to completely cure a fungal infection within 100 to 150 days after the beginning of the treatment. (Specification, page 15). Thus, Applicant respectfully submits that this unexpected result is sufficient to rebut any presumption of obviousness, and thus, requests that this rejection be withdrawn.

II. The Rejection Over Samour, Ippen and Wohlrab Should Be Withdrawn

On pages 7-9 of the Office Action, claims 1-2 and 4 are rejected over Samour in view of Ippen and U.S. Patent No. 6,719,986 to Wohlrab et al. (“Wohlrab”). It appears that, in addition to the rejection of claims 1-2 discussed above, Wohlrab is added to show that “the use of hyaluronate lyase as permeation enhancing agent” in topical formulations, as recited by claim 4, would have been obvious. (Office Action, page 8). Applicant respectfully disagrees.

At the outset, Applicant respectfully points out that claims 1-2 and 4 are unobvious and patentable for the reasons same as those discussed above in connection with Samour and Ippen. In addition, Applicant respectfully submits that claim 4 is separately patentable because “the use of hyaluronate lyase as permeation enhancing agent” does indeed provide patentable distinction to claim 4 over prior art.

As the Examiner recognizes, Wohlrab discloses that hyaluronate lyase “as permeation enhancing agent in topical agent.” (Office Action, page 8). In this regard, Wohlrab shows the efficacy of hyaluronate lyase in penetrating into human skin. (Wohlrab, FIGs 1 and 2 and description thereof). Thus, Wohlrab teaches that hyaluronate lyase is a skin penetration enhancer. Yet, Samour, the primary reference cited in the Office Action, discloses that “solvents with proven efficacy as skin ‘penetration enhancers’ show little promise as enhancers of nail permeability.” (Samour, col. 2, lines 39-47) (emphasis added). Indeed, this is precisely why Samour provides specific permeation enhancers, *i.e.*, C₇-C₁₄-hydrocarbyl substituted 1,3-dioxolane, C₇-C₁₄-hydrocarbyl substituted 1,3-dioxane and C₇-C₁₄-substituted acetal, for use in its formulations. Thus, in view of the fact that Wohlrab teaches hyaluronate lyase as a skin penetration enhancer, Samour would have taught those skilled in the art away from using hyaluronate lyase as a permeation enhancer in nail lacquer formulation.

For these reasons, Applicant respectfully submits that claims 1-2 and 4 are not obvious over Samour, Ippen and Wohlrab, and thus, respectfully requests that this rejection be withdrawn.

III. The Rejection Over Samour, Ippen and Gyurik Should Be Withdrawn

On pages 9-11 of the Office Action, claims 1-2, 11 and 14-15 are rejected over Samour, in view of Ippen and WO 01/60325 by Gyurik (“Gyurik”). In particular, based on Example 1 of Gyurik, which purportedly discloses “a nail lacquer composition comprising” various ingredients recited by claims 11 and 14-15, it is alleged that the claims would have been obvious to “incorporate the specific types of [ingredients described in Gyurik] because they are conventionally known additives in a nail lacquer composition as also demonstrated by Gyurik.” (Office Action, pages 10-11). Applicant respectfully disagrees.

First, Applicant respectfully point out that claim 11, which depend from claim 1 or 2, cannot be obvious for the reasons same as those discussed above in connection with claims 1 and 2. Applicant further submits that claims 11 and 14-15 are not obvious over the combination of references cited in the Office Action for the following additional reasons.

As the Examiner recognizes, the formulation described in Gyurik employs clotrimazole as an active agent, which is completely different from the currently claimed 2-aminothiazole compounds. Therefore, in view of the fact that those skilled in the art would have thought that 2-aminothiazoles would not be compatible with polar ingredients (such as Eudragit and oxacyclohexadecan-2-one) due to the potential binding issue discussed above, there would have been no reason to “incorporate the specific types of” ingredients described in Gyurik. In fact, Applicant respectfully submits that there would have been ample reason not to use the specific types of ingredients described in Gyurik in view of the potential binding issue.

In addition, Samour’s teaching that “solvents with proven efficacy as skin ‘penetration enhancers’ show little promise as enhancers of nail permeability” would have discouraged those skilled in the art from using, for example, oxacyclohexadecan-2-one (a known skin penetration enhancer) in nail lacquer formulation.

Thus, for at least the reasons given above, Applicant respectfully submits that claims 1-2, 11 and 14-15 are unobvious over Samour, Ippen and Gyurik, and thus, respectfully requests that this rejection be also withdrawn.

C. Conclusion

In light of the above amendments and remarks, Applicant respectfully requests that the Examiner reconsider this application with a view towards allowance.

No fees, other than that required for the extension of time, are believed due at this time. However, please charge any required fees, or credit any overpayments, to Jones Day Deposit Account No. 50-3013.

Respectfully submitted,

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